Risk of gastric cancer in pneumoconiotic coal miners and the effect of respiratory impairment

G M H Swaen, J M M Meijers, J J M Slangen

Abstract

***Objectives*—This study was carried out to investigate the mortality patterns in a group of 3790 coal miners. The study population had abnormal chest *x* ray films at a routine medical examination that was performed in the 1950s.**

***Methods*—The total group of 3790 coal miners was followed up for mortality up to 1 January 1992. Causes of death, determined and coded at time of death, were traced with help from the Central Bureau of Statistics.**

***Results*—Total mortality in this group of coal miners with abnormal chest *x* ray films was significantly higher than expected (SMR 127·1, 95% CI 122·5–131·6), mainly a reflection of the increase in mortality from non-malignant respiratory disease (SMR 411.0, 95% CI 382·3–441·3). Mortality from gastric cancer was also significantly increased (SMR 147·5, 95% CI 122·3–176·3). This risk of mortality from gastric cancer was confined to workers with no pneumoconiosis or only a mild form. Despite the strong relation to duration of employment and pneumoconiosis the group of workers with more severe manifestations of pneumoconiosis did not experience an excess in mortality from gastric cancer.**

***Conclusion*—This study confirms the earlier reported risk of gastric cancer in coal miners. Also it confirms the hypothesis that this risk of gastric cancer is limited to workers with a mild degree of pneumoconiosis or none. In workers with severe forms of pneumoconiosis the pulmonary clearance system is impaired in such a way that the inhaled coal dust does not reach the digestive tract.**

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During their work underground coal miners are continuously exposed to coal dust particles. A proportion of these coal dust particles will reach the respiratory system, where they can have adverse health effects. There is no doubt that prolonged exposure to these respirable particles imposes a threat to the respiratory health of the exposed workers. Coal workers' pneumoconiosis (CWP) is a well documented occupational disease in underground coal miners, for which the coal dust particles are the responsible agent.[1 2] There is still considerable debate about the underlying mechanism that is responsible for the genesis of pneumoconiosis.[3]

Coal dust contains agents that are also suspected of having other long term effects on the lungs. Silica for instance is regarded by the International Agency for Research on Cancer (IARC) as probably carcinogenic to humans, perhaps capable of inducing lung cancer.[4] Coal dust also contains various well recognised carcinogenic organic compounds, such as benzo(a)pyrene, chrysene, and benzo(a)-anthracene derivatives and some inorganic carcinogens—mostly trace metals like cadmium, chromium, and nickel in various concentrations.[5] Most epidemiological investigations on lung cancer have found rates appreciably lower than those expected in coal miners. This was also concluded by an IARC working group.[4] An increased risk of gastric cancer has consistently been found in many mortality studies of coal miners.[6] Inhaled coal dust can reach the digestive tract by means of the pulmonary clearance system. This route of exposure may be responsible as increased mortality from gastric cancer was found in several follow up studies of coal miners.[7 8]

Various hypotheses have been postulated to explain the origin of the increased rate of gastric cancer in coal miners. Some researchers have argued that the increased risk of gastric cancer is mainly due to differences in susceptibility, lifestyle, and socioeconomic status of coal miners in comparison with control populations.[9] Others pointed to a more direct relation between occupational exposure to coal dust and stomach cancer.[10] The inhaled coal dust is swallowed and introduced in the acidic environment of the stomach, where it may interact with nitrosating agents, such as nitrite. Experimental studies in the salmonella/microsome assay system have confirmed that this leads to the formation of compounds that have mutagenic activity.[10]

It was proposed by Meyer *et al*[11] and Ames *et al*[9] that a good respiratory clearance mechanism in exposed workers may be an intermediate risk factor for gastric cancer in these workers. In workers with an unaffected clearance mechanism inhaled coal dust can be readily transported to the digestive tract, whereas a defective clearance system would prevent coal dust from reaching the digestive tract.

Stimulated by the availability of data a study was carried out to further investigate

Table 1 Baseline characteristics of 3790 coal miners who participated in extensive medical examinations

	Grade of pneumoconiosis			
	0–1 *n (%)*	*2–5* *n (%)*	*6–7* *n (%)*	*Total*
Underground employment (y):				
<10	4 (14·8)	19 (70·4)	4 (14·8)	27
10–19	54 (16·2)	231 (69·1)	49 (14·7)	334
20–29	99 (7·7)	977 (76·0)	209 (16·3)	1285
30–39	223 (12·0)	1390 (74·7)	247 (13·3)	1860
⩾40	43 (15·1)	192 (67·6)	49 (17·3)	284
Age at examination:				
<40	31 (10·8)	228 (79·2)	29 (10·0)	288
40–49	82 (6·5)	969 (77·1)	206 (16·4)	1257
50–59	233 (13·0)	1324 (73·8)	237 (13·2)	1794
⩾60	77 (17·1)	288 (63·9)	86 (19·0)	451
Total	423 (11·2)	2809 (74·1)	558 (14·7)	3790

this hypothesis. Between 1902 and 1974 coal mining was the main industrial activity in the southern part of The Netherlands. At its peak the coal mines employed over 50 000 coal miners. Triggered by concern for the long term health effects of underground coal mining a special lung institute was established to detect and prevent CWP. In the 1950s several cross sectional surveys were carried out within this programme. Coal miners with over 10 years of underground employment were invited to attend pulmonary screening programmes. Of the workers attending these surveys 27% showed pneumoconiotic lesions on examination of *x* ray films.[12] The data set compiled during these examinations formed the basis of this longitudinal study. The aim of the present investigation was to determine the long term mortality patterns of gastric cancer in this group and identify the relation between duration of exposure to coal dust, the respiratory clearance mechanism, and gastric cancer.

Materials and methods

The initial study population was derived from the files of all the coal miners who participated in the cross sectional respiratory health surveys carried out by the collaborative lung institute during the 1950s. The subjects of our study were invited for a further pulmonary examination, because they had radiological signs of respiratory disease. For a total of 3790 coal miners sufficient data were still available from the files of the lung institute to be relevant for analysis. During the medical examination in the 1950s several characteristics was recorded. Among these were demographic data, height, weight, job history, and diseases and complaints of the respiratory system. For classification of CWP a Modified International Labour Organisation (ILO) classification was used. The classification was made by a specially trained pulmonary specialist. The classification system consisted of the following categories: other abnormalities (0–1), simple pneumoconiosis (2–5), or progressive massive fibrosis (6–7). This classification was based on the presence on the lung radiograph of (micro)nodules, confluent opacities, and massive tumours, respectively. Currently there is no validation available for the classifications made by the pulmonary specialist about 40 years ago. It must be kept in mind that the level of disability compensation paid to each worker depended on this medical examination and classification. "Other abnormalities (group 0–1)" indicate abnormal chest *x* ray films not related to CWP, for instance pneumonia scarring or abnormal *x* ray film caused by tuberculosis. Table 1 shows age at examination, total duration of underground employment, and grade of pneumoconiosis at baseline. Lung function was measured by trained personnel, with a wet spirometer. The forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were analysed. The measured FEV_1 and FVC were compared with standard values for specific age groups that were generally accepted at the time of examination in the 1950s. The lung impairment, defined as a decrease in FEV_1 ($\leqslant$70% of the standard value) and FVC ($\leqslant$80% of the standard value), was used as a measure of the impairment of the respiratory clearance.[13] Most of the subjects were over 40, had worked underground for more than 20 years, and had at least pneumoconiosis grade 2. All workers enrolled in the study were followed up for mortality. The end of the follow up was set at 1 January 1992. The Netherlands is covered by a system of population registries. When a person moves from one municipality to another, this is recorded in both registries. These municipal population registries facilitate the mortality follow up. When a person has died a death certificate containing the underlying cause of death is filed at the Central Bureau of Statistics (CBS). After having complied with strict privacy regulations, researchers can obtain the cause of death distributions for specific groups and subgroups. Table 2 gives the frequency distributions of the end points of the follow up.

Table 2 End points of mortality follow up until 1 January 1992 of 3790 coal miners in the Netherlands

	N (%)
Total population	3790 (100)
Alive on 1 January 1992	709 (18·71)
Emigrated	21 (0·55)
Lost to follow up	119 (3·14)
Died before 1 January 1992	2941 (77·60)
Cause of death known	2900 (98·61)
Cause of death not known	41 (1·39)
Person-years of follow up	77 440·75

For 96·3% of the total study population the vital status on 1 January 1992 was obtained. As the average duration of follow up was 20·4 years this achievement was regarded as satisfactory. For only 1·4% of the deaths no cause of death could be obtained from the CBS. In the analysis no adjustments were made for deaths for which no cause of death was available. This may have led to a slight underestimation of the relative risk under the assumption that the proportion of deaths without a known cause was larger in the study population than in the total Dutch male population. To take into account the specific study aims the total study population was stratified according to the variables relevant to these study aims. These variables were: duration of employment, severity of CWP, FEV_1 under or over 70% of the expected value, and FVC_1 under or over 80% of the expected value, based on age specific normal values that were in general use at that time.

In comparison with current exposure standards the coal miners were exposed to high dust concentrations. Several industrial hygiene surveys were carried out in the past. The average of the total gravimetric dust samples was 27 mg/m^3 with an average of 5% quartz. Although there were differences in industrial hygiene between pits it is likely that workers of all coal mines were exposed to coal dust concentrations of 20 mg/m^3 and over. It is also clear that the exposure concentrations have varied from job to job. The coal miners who worked close to the coal face were exposed to dust containing relatively more coal particles than those who were responsible for tunnelling work on the sides of the coal face and through rock.

STATISTICAL ANALYSES

To adjust for differences in age distribution, period, and length of follow up an indirect standardisation procedure was used. National age, sex, period, and cause specific mortality rates were applied to the study population or subgroups. Age and interval specific person-years were calculated by means of the computer program designed by Peto.[14] These person-years multiplied by the national mortality rates produced the expected number of deaths for each cause of death in each subgroup. 95% Confidence intervals (95% CIs) were calculated with the method proposed by Breslow and Day.[15] As the cohort was compiled by means of the medical dossiers from the respiratory health examination in the 1950s, only person-years were included since that medical examination. Person-years before that date were not counted as person-years at risk. Person-years were counted up to the date that an end point of the follow up was reached, being the last date of the follow up (1 January 1992), emigration date, date of death, or date of loss to follow up.

The study population was stratified into several subgroups according to duration of employment, severity of pneumoconiosis, time interval, and lung function as measured by the FVC and FEV_1.

Table 3 Cause specific mortality and SMRs in 3790 coal miners in The Netherlands

Causes of death	*Observed*	*Expected*	*SMR*	*(95% CI)*
All causes of death	2941	2314·3	127	(123–132)**
Infectious diseases	57	15·2	374	(284–485)**
All malignant neoplasms	668	690·5	97	(90–104)
Circulatory diseases	1152	1061·4	109	(102–115)**
Non-malignant respiratory diseases	761	185·2	411	(382–441)**
Non-malignant diseases of digestive organs	59	71·6	82	(63–106)
Residual non-malignant diseases	132	209·3	63	(53–75)*
All external causes of death	71	81·2	87	(68–110)
Malignancies:				
Buccal cavity, pharynx	1	6·4	16	(0–79)*
Oesophagus	7	11·3	62	(25–127)
Stomach, small intestine	120	81·4	147	(122–176)**
Large intestine	35	40·9	86	(60–119)
Rectum	31	23·8	130	(89–185)
Biliary passage, liver	6	12·5	48	(17–104)
Pancreas	21	29·6	71	(44–108)
Nose and sinuses (160)	2	1·0	205	(30–714)
Larynx (161)	6	6·2	98	(36–211)
Lung (162–165)	272	266·7	102	(90–115)
Bone	2	2·0	99	(11–345)
Connective tissue	1	1·7	60	(1–303)
Skin	5	4·2	118	(38–274)
Prostate	40	58·2	69	(49–94)
Testis, male genitals	2	1·8	110	(12–383)
Bladder, urinary organs	9	26·0	35	(16–66)*
Brain	8	7·5	107	(46–211)
Lymphosarcoma	8	4·8	167	(72–328)
Hodgkin's disease	4	3·0	135	(36–341)
Lymphomas	7	5·3	133	(53–273)
Multiple myeloma	6	9·7	62	(22–133)
Leukaemia (total)	17	17·2	99	(57–158)
Non-specified malignant neoplasms	29	30·1	96	(65–139)
Benign neoplasms	4	2·4	164	(44–415)

*P < 0·05; **P < 0·05.

Results

The total mortality in this cohort of coal miners with abnormal chest *x* ray films (indicating CWP or other pulmonary pathology) was higher than expected, compared with national mortality rates. Table 3 shows the results of this comparison. Several mortality rates from subgroups with pulmonary disease, such as non-malignant respiratory diseases (SMR 411) and infectious diseases (SMR 374) were raised (the infectious diseases included deaths from tuberculosis). The excess in total mortality is mainly explained by the mortality from non-malignant respiratory disease. An excess of 576 deaths was found from non-malignant respiratory diseases compared with the total excess of 627 deaths regardless of the cause. Although the total number of deaths due to neoplasms was lower than expected, gastric cancer was significantly increased. Deaths from gastric cancer were 120 observed, compared with 81·4 expected, giving an SMR of 147·5 (95% CI 122·5–176·3).

The total population was stratified according to calender period. In the period before 1970, 54 study subjects had died from gastric cancer compared with 32·5 expected (SMR: 166, 95% CI 124·9–217·0). Between 1970 and 1980 43 had died of gastric cancer with 26·6 expected (SMR 161·4, 95% CI 116·8–217·4). The time interval after 1980, however, showed no increase in mortality from gastric cancer (23 deaths observed *v* 22·3 expected).

A relation was present between duration of exposure (underground employment) and response (the SMR for gastric cancer). Workers with 20 years or less underground had an SMR for gastric cancer of 113·3 (95% CI 36·5–262·3). The SMR was 138·2 (95%

Table 4 SMRs for total mortality and mortality from gastric cancer by severity of pneumoconiosis and lung function characteristics (FVC, FEV_1)

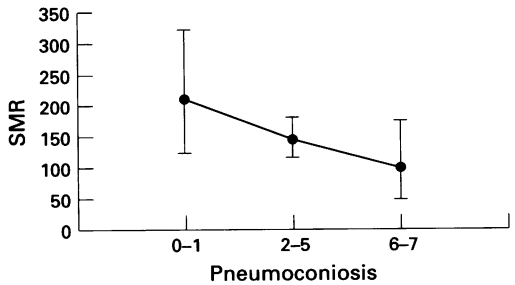
Grade of pneumoconiosis	*SMR total mortality (95% CI)*	*SMR gastric cancer (95% CI)*
0–1	137·0 (122·9–152·3)	206·6 (124·3–322·4)
2–5	122·4 (117·3–127·7)	147·4 (118·5–181·2)
6–7	145·4 (132·2–159·4)	98·8 (49·2–176·4)
Lung function:		
FVC < 80%	167·0 (151·7–183·5)	71·7 (28·7–147·0)
FVC > 80%	120·8 (115·9–125·7)	154·5 (126·4–187·0)
FEV_1 < 70%	163·9 (154·8–173·4)	126·4 (88·0–175·8)
FEV_1 > 70%	107·1 (101·9–112·5)	154·6 (122·0–193·3)
Duration of underground employment:		
≤20 y	118·3 (101·1–137·5)	113·3 (36·5–262·3)
20–29 y	126·8 (118·6–135·4)	138·2 (94·5–195·0)
≥30 y	128·1 (122·3–134·0)	154·3 (122·9–191·2)
Total group	127·1 (122·5–131·8)	147·4 (122·2–176·3)

CI 94·5–195·0) in workers with underground employment between 20 and 30 years. Workers who had been employed underground for 30 years or more had an SMR for gastric cancer of 154.3 (95% CI 122·9–191·2). This relation between duration of exposure and response was significant in the test for trend proposed by Breslow and Day.[15]

The severity of pneumoconiosis was inversely related to the risk of gastric cancer. In the group without CWP(0–1) the risk of gastric cancer was doubled (SMR 206·6, 95% CI 123·3–322·4). In the group with minor CWP the risk of gastric cancer was about half (SMR 147·4, 95% CI 118·5–181·2), whereas there was no apparent excess of mortality from gastric cancer in the group with severe CWP (SMR 98·8, 95% CI 49·2–176·4), despite their longer exposure to coal dust. This inverse trend was significant ($P < 0·01$), when tested as proposed by Breslow and Day.[15]

The relation between risk of gastric cancer and lung function, as a surrogate for respiratory impairment, was investigated by stratifying the FVC and FEV_1. Table 4 shows the SMRs by severity of pulmonary impairment. Similar trends were found after stratification by FEV_1 and FVC. In the group of coal miners with an FVC smaller than 80%, the mortality from gastric cancer was even lower than expected.

Next the study population was stratified according to duration of employment underground and severity of pneumoconiosis. The figure shows the results of this stratified analysis. Apparently the workers with underground employment of 30 years or more and only a mild form of pneumoconiosis or none have the highest SMR for gastric cancer.



SMRs of gastric cancer for three subgroups with different severities of pneumoconiosis (for exact data, see table 4).

Similar analyses were carried out to investigate relations between duration of exposure, pulmonary disease, and lung cancer. None of these factors seemed to be related to mortality from lung cancer.

Discussion

In this study several increased mortality rates were found in the 3790 coal miners with abnormal *x* ray films. The total mortality in this group was significantly higher than expected based on the mortality rates of the general male population. This increase resulted mainly from increased mortality rates of non-malignant respiratory disease. Apart from this risk an increased SMR for gastric cancer was also noted. The SMR for gastric cancer was 147·5 (95% CI 122·2–176·3). Overall, a relation between duration of exposure to coal dust and the risk of gastric cancer exists. There is also an inverse relation between the grade of pneumoconiosis and gastric cancer. This is consistent with an impaired respiratory clearance in miners with severe pneumoconiosis.

Inhaled coal dust may reach the stomach by normal pulmonary clearance and may account for the association of stomach cancer with occupational exposure to coal dust. Meyer *et al*[11] have postulated that people whose pulmonary clearance mechanisms are impaired do not have an increased risk of stomach cancer, as the coal dust does not reach the stomach, but remains in the lungs. This study provides support for this hypothesis.

Coal miners with a normal lung function showed the highest risk of gastric cancer. This is understandable, as the amount of coal dust that eventually reaches the stomach is highest in these miners. The risk of gastric cancer in this group is much higher than in the group with a severe degree of pneumoconiosis, which is associated with high exposure to coal dust. Without interference of pneumoconiosis in the pathway by which coal dust reaches the gastrointestinal tract, the cases of more severe pneumoconiosis would be expected to form a group at high risk of gastric cancer, as these are the miners likely to have experienced the highest exposures to coal dust. This is not the case. The results of this study support the hypothesis put forward by Meyer *et al.*[11]

Unfortunately the validity of the CWP classification cannot be assessed retrospectively. Classification of CWP was performed by a specially trained pulmonologist and the degree of CWP determined was important for the level of disability benefits received by the workers.

A second shortcoming of the study is the lack of individual exposure information. Such individual exposure information would have provided an opportunity for a more refined statistical analysis.

Despite these limitations in the data, the findings of this study include the intermediary

role of pulmonary clearance in the process by which coal dust reaches the gastrointestinal tract, and support the hypothesis that coal dust is a causative agent for gastric cancer in coal miners.

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